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Case Report

Low-Grade B Cell Lymphoproliferative Disorder Masquerading as Chronic Rhinosinusitis

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Abstract: Chronic rhinosinusitis (CRS) is one of the most common persistent disorders of the developed world, requiring input from various specialists including primary care physicians, otolaryngologists, respiratory physicians, and allergologists. B-cell lymphoproliferative disorders (BLPDs) are a heterogenous group of malignant conditions defined by an accumulation of mature B lymphocytes in the bone marrow, blood, and lymphoid tissues. We present a case report of an elderly man with rhinosinusitis-like symptoms and atypical features prompting further investigations that culminated in a diagnosis of BLPD.

Keywords: chronic rhinosinusitis; B-cell lymphoproliferative disorder



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1. Introduction

Chronic rhinosinusitis (CRS) is one of the most common persistent disorders of the developed world, requiring input from various specialists including primary care physicians, otolaryngologists, respiratory physicians, and allergologists [1]. Current international guidelines recommend that diagnosis is made by clinicians on the basis of symptoms such as nasal blockage, discharge, facial pressure, and loss of smell for at least 12 weeks [2]. However, the diagnostic work up can be fraught with difficulty, especially when attempting to differentiate between CRS and allergic and nonallergic rhinitis on symptoms alone. Additionally, not all patients with CRS criteria will have evidence of disease on nasal endoscopy and CT imaging [2].

Based on high quality evidence, medical therapy with long term nasal corticosteroids, short courses of oral corticosteroids, and/or nasal irrigation with isotonic saline or Ringer's lactate are effective in treating CRS [2]. Dupilumab (anti-IL4 α) is the only monoclonal antibody approved for the treatment of CRS with nasal polyps (CRSwNP) at present. Two studies have demonstrated efficacy of intravenous mepolizumab (anti-IL5) 750 mg q4w on reducing the need for nasal polyp surgery and total polyp score [3,4] but at the current subcutaneous licensed dose of 100 mg q4w, our experience has shown a clear disconnect in response between severe eosinophilic asthma and CRSwNP [5]. Surgical management is usually indicated when CRSwNP is refractory to medical therapy [2].

B-cell lymphoproliferative disorders (BLPDs) are a heterogenous group of malignant haematological conditions with a significantly higher incidence in individuals with primary or secondary immunodeficiency [6]. Diagnosis is usually made on the basis of clinical features such as enlarged lymph nodes or splenomegaly and excess fatigue and/or apparent cytopenia and lymphocytosis on a full blood count [7]. Morphological examination demonstrating a lymphocytic increase or abnormality would prompt further immunophenotypic investigations. Multiparameter flow cytometry on peripheral blood or bone marrow is a rapid and efficient tool for the diagnosis of BLPDs [7].

2. Case

A 72-year-old man was referred by his general practitioner for chronic bilateral nasal congestion, worse at night, and purulent nasal secretions predominantly in the morning. In addition to multiple courses of antibiotics, he had previously tried fluticasone furoate, mometasone furoate, and beclomethasone dipropionate nasal sprays to no avail. He retained his sense of smell and denied post-nasal drip, sneezing, breathlessness, or cough. He had no history of excess fatigue, weight loss, or night sweats. His past medical history included essential hypertension for which he was taking perindopril 2 mg once daily (OD) and a previous cerebral infarction treated with clopidogrel 75 mg OD. He is an ex-smoker with no relevant family history.

Nasal endoscopy (30° oblique rigid Hopkins 3.0 mm) performed in our rhinology mega-clinic revealed an oedematous friable bleeding nasal mucosal surface with significant crusting but no polyps per se. Biopsy samples were taken from the middle turbinate and crusting was debrided. Nasal douching with saline/bicarbonate was recommended, and he was treated with concurrent azithromycin 500 mg OD and prednisolone 25 mg OD for 5 and 7 days, respectively, pending further results.

Initial laboratory results and subsequent lymphocyte surface marker analysis are presented in Table 1. Protein electrophoresis identified two monoclonal bands consistent with IgM lambda and kappa bands quantifiable at 10 g/L. CT sinus scan (Figure 1) revealed mucosal disease predominantly affecting the ethmoid bullae and ostiomeatal complex, with a Lund Mackay score of 12. Apart from minor basal atelectasis, chest X-ray was normal. Histopathology subsequently revealed chronic non-specific inflammatory changes with mixed microbial flora abundant in gram-positive cocci.

Table 1. Laboratory results and lymphocyte surface marker analysis.

White Blood Cells ($\times 10^9$ /L)	9.8	Corr. Calcium (mmol/L)	2.44
Haemoglobin (g/L)	136	C-reactive protein (mg/L)	<4
Haematocrit (%)	41.3	Sodium (mmol/L)	141
Platelets ($\times 10^9$ /L)	328	Potassium (mmol/L)	4.8
Neutrophils ($\times 10^9$ /L)	5.4	Urea (mmol/L)	6.4
Lymphocytes ($\times 10^9$ /L)	3.5	Creatinine (μ mol/L)	86
Eosinophils ($\times 10^9$ /L)	0.14	PR3/MPO antibodies	negative
Plasma viscosity (mPa.s)	1.99 \uparrow	CTD screen	negative
Total bilirubin (μ mol/L)	5	RAST to ABCDH	negative
ALT (U/L)	25	RAST to grass	weakly positive
ALP (U/L)	110	Total IgE (kU/L)	89.5
Albumin (g/L)	36	IgG (g/L)	9.94 (NR 5.5–13)
Pneumococcal ab (mg/L)	52.64	IgA (g/L)	1 (NR 0.5–4)
		IgM (g/L)	10.2 \uparrow (NR 0.5–2.5)
CD3 (%)	88.57 \uparrow	CD19 (%)	3.53
CD3 ($\times 10^6$ /L)	2922 \uparrow	CD19 ($\times 10^6$ /L)	116
CD4 (%)	32.94 \uparrow	NK cells (%)	6.88
CD4 ($\times 10^6$ /L)	1087	NK cells ($\times 10^6$ /L)	227
CD8 (%)	53.6 \uparrow	CD4/CD8 ratio	0.62 \downarrow
CD8 ($\times 10^6$ /L)	1769 \uparrow		

A = aspergillus fumigatus; ALP = alkaline phosphatase; ALT = alanine aminotransferase; B = silver birch; C = cat dander; CD = cluster of differentiation; CTD = connective tissue disease; D = dog dander; H = house dust mite; MPO = myeloperoxidase; NK = natural killer; NR = normal range; PR3 = proteinase-3; RAST = radioallergosorbent testing for specific IgE. \uparrow and \downarrow denote values outside NR.

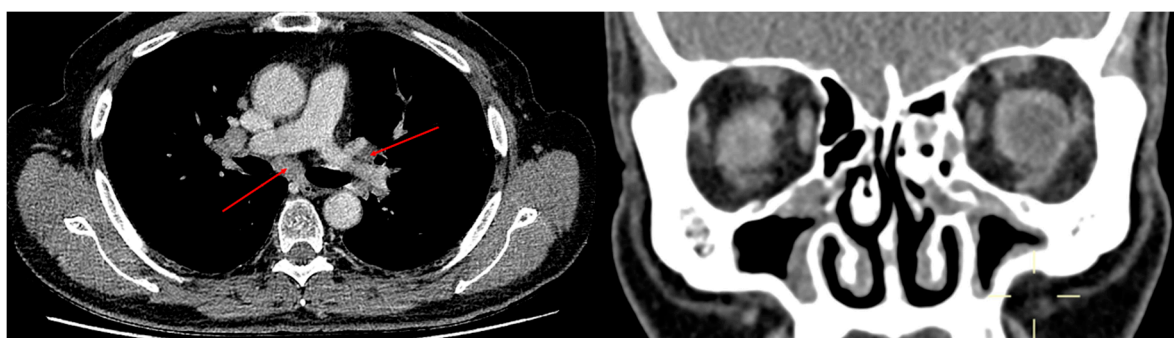


Figure 1. Transverse CT chest image with arrows indicating mediastinal and hilar lymphadenopathy. Coronal CT sinus image depicting disease affecting the ethmoid bullae and ostio-meatal complex.

Our patient was consequently referred to haematology where on physical examination there was no clinical evidence of palpable lymphadenopathy or hepatosplenomegaly. A CT chest-abdomen-pelvis scan (Figure 1) identified significant mediastinal and hilar lymphadenopathy and the combination of serum and radiological findings in turn made the clinical diagnosis of B-cell lymphoproliferative disorder (BLPD).

3. Discussion

In this case report, we present a patient referred from primary care for CRS without nasal polyposis and suspicious atypical features who was subsequently diagnosed with low grade BLPD. To our knowledge, although there have been case series on localised sinonasal lymphoma [8,9], we have not yet encountered a case report of BLPD masquerading as CRS.

While the diagnosis of BLPD was clinical, the value of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) of mediastinal and hilar lymph nodes in the diagnosis of lymphoma is controversial [10] and hence a negative result would likely still mandate surgical mediastinoscopy confirmation. In the absence of B symptoms or abnormal full blood count, a watch and wait strategy is usually employed for low grade BLPDs and therefore no bone marrow or lymph nodes were sampled in our patient, to avoid unnecessary additional risk.

The abundance of gram-positive cocci is likely to infer chronic staphylococcal infection, which in turn is highly suggestive of immunosuppression. Although the acute abundance of gram-positive cocci commonly infers nasal colonisation with *Streptococcus pneumoniae*, failure to respond to recurrent courses of antibiotic therapy likely results in a selection pressure towards treatment resistant organisms such as *Staphylococcus aureus* [11]. Risk factors for *S. aureus* nasal colonisation depends on host factors but is more frequent in conditions that result in immunosuppression such as in patients infected with human immunodeficiency virus (HIV) or those who are diabetic and undergoing dialysis [12]. The combination of immunosuppression, IgM paraproteinaemia, and extensive mediastinal and hilar lymphadenopathy is probably sufficient to make a clinical diagnosis of BLPD.

The key learning point here is that although nasal crusting is a frequently encountered clinical feature that often requires no specific treatment, it is nevertheless crucial for the clinician to identify the small number of cases that are due to a potentially wide differential diagnosis including systemic inflammatory disorders such as vasculitis, malignancy, and infection, amongst others [13]. Clinicians should have a high index of clinical suspicion and our usual practice should be to check serum protein electrophoresis and immunoglobulins in all patients presenting with CRS-like symptoms and signs of immunosuppression as it may lead to an earlier diagnosis and potentially better outcome for patients.

4. Conclusions

Patients with chronic rhinosinusitis who present with atypical clinical features such as nasal crusting and treatment resistant organisms may have underlying immunosuppres-

sion. Identifying this in a timely manner with further focused investigations may lead to earlier diagnoses and better outcomes for patients.

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